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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/710,419	11/09/2000	John M. Tomich	30917	5692

23589 7590 06/17/2002

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EXAMINER
MURPHY, JOSEPH F

ART UNIT	PAPER NUMBER
1646	

DATE MAILED: 06/17/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/710,419	Applicant(s) TOMICH ET AL.	
	Examiner Joseph F Murphy	Art Unit 1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 April 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *18-36 and 41-46* is/are pending in the application.

4a) Of the above claim(s) *18-29 and 41-46* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *30-36* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 5 .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *Sequence Comparison A* .

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of Group LXXI, claims 30-36, drawn to a method of altering water flux across a membrane comprising SEQ ID NO: 13 in Paper No. 4/15/2002 is acknowledged. The traversal is on the ground(s) that the peptides are derived from SEQ ID NO: 1 and share a common function. This is not found persuasive because the peptides of SEQ ID NO: 4-47 have dissimilar structures which would entail a separate search for each peptide, thus placing a burden on the Examiner.

The requirement is still deemed proper and is therefore made FINAL. Claims 18-29, 37-46 are withdrawn from further consideration pursuant to 37 CFR 1.142(b). Claims 30-36 are under consideration.

Claim Rejections - 35 USC § 112 first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 30-36 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of altering the flux of water across a membrane with a peptide of SEQ ID NO: 13, does not reasonably provide enablement for a method of altering the flux of water across a membrane with a variant peptide of SEQ ID NO: 13 having at least about 35%, 50%, or 65% amino acid sequence homology to SEQ ID NO: 13. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

Claims 30-36 are overly broad in the recitation of "having at least about 35%, 50%, or 65% amino acid sequence homology to SEQ ID NO: 13" since insufficient guidance is provided as to which of the myriad of polypeptide species encompassed by the claim will retain the characteristics of altering water flux across a membrane. It is known in the art that even single amino acid changes or differences in the amino acid sequence of a protein can have dramatic effects on the protein's function. For example, Voet et al. (1990) teaches that a single Glu to Val substitution in the beta subunit of hemoglobin causes the hemoglobin molecules to associate with one another in such a manner that, in homozygous individuals, erythrocytes are altered from their normal discoid shape and assume the sickle shape characteristic of sickle-cell anemia, causing hemolytic anemia and blood flow blockages (pages 126-128, section 6-3A and page 230, column 2, first paragraph).

There is insufficient guidance provided in the specification as to how one of ordinary skill in the art would practice a method of altering the flux of water across a membrane with a variant peptide of SEQ ID NO: 13 having at least about 35%, 50%, or 65% amino acid sequence homology to SEQ ID NO: 13. See In re Wands, 858 F.2d at 737, 8 USPQ2d at 1404. The test of enablement is not whether any experimentation is necessary, but whether, if experimentation is necessary, it is undue. The factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue" include, but are not limited to: (1) the breadth of the claims; (2) the nature of the invention; (3) the state of the prior art; (4) the level of one of ordinary skill; (5) the level of predictability in the art; (6) the amount of direction provided by the inventor; (7) the existence of working examples; and (8) the quantity of

experimentation needed to make or use the invention based on the content of the disclosure. Given the breadth of claims 30-36 in light of the predictability of the art as determined by the number of working examples, the level of skill of the artisan, and the guidance provided in the instant specification and the prior art of record, it would require undue experimentation for one of ordinary skill in the art to make and use the claimed invention.

Claims 30-36 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

These are genus claim. The specification and claim do not indicate what distinguishing attributes shared by the members of the genus. The specification and claim do not place any limit on the number of amino acid substitutions, deletions, insertions and/or additions that may be made to SEQ ID NO: 13. Thus, the scope of the claim includes numerous structural variants, and the genus is highly variant because a significant number of structural differences between genus members is permitted. Although the specification states that these types of changes are routinely done in the art, the specification and claim do not provide any guidance as to what changes should be made. Structural features that could distinguish compounds in the genus from others in the protein class are missing from the disclosure. No common structural attributes identify the members of the genus. The general knowledge and level of skill in the art do not supplement the omitted description because specific, not general, guidance is what is

needed. Since the disclosure fails to describe the common attributes or characteristics that identify members of the genus, and because the genus is highly variant, SEQ ID NO: 13 alone is insufficient to describe the genus. One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus. Thus, applicant was not in possession of the claimed genus.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 30-36 are rejected under 35 U.S.C. 102(b) as being anticipated by WO 9726905 (Iwamoto et al.).

Iwamoto et al. discloses peptides which can alter the flux of water across a membrane. The peptide disclosed in Iwamoto is 100% identical to the peptide of SEQ ID NO: 13 of the instant application (see Sequence Comparison A, attached.). The peptides are water soluble to at least 10 mM and enables anions to be transported through a membrane of an epithelial cell when they are embedded in the membrane (page 6, lines 10-19). The peptides exhibit at least 50% helical content (6, lines 10-19). The channel assembly can be used to alter the flux of water across an epithelial cell, particularly for treatment of cystic fibrosis (where affected cells are in the airway, pancreatic duct or epididymis). Iwamoto discloses methods of using the peptides to alter the flux of water across a membrane (page 14, lines 5-34) thus claims 30-36 are anticipated.

Conclusion

No claim is allowed.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph F. Murphy whose telephone number is 703-305-7245. The examiner can normally be reached on M-F 7:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler can be reached on 703-308-6564. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-308-0294 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Joseph F. Murphy, Ph. D.
Patent Examiner
Art Unit 1646
June 11, 2002

DAVID S. ROMEO
PRIMARY EXAMINER

Sequence Comparison A

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RESULT   1
AAW22803
ID   AAW22803 standard; peptide; 23 AA.
XX
AC   AAW22803;
XX
DT   13-MAR-1998  (first entry)
XX
DE   Channel-forming M2GlyR peptide 1.
XX
KW   Channel-forming peptide; channel assembly; epithelial cell; treatment;
KW   cystic fibrosis; polycystic kidney disease; anion transportation; M2GlyR.
XX
OS   Synthetic.
OS   Homo sapiens.
XX
PN   WO9726905-A1.
XX
PD   31-JUL-1997.
XX
PF   27-JAN-1997;   97WO-US01103.
XX
PR   24-JAN-1997;   97US-0789155.
PR   25-JAN-1996;   96US-0591381.
PR   23-JAN-1997;   97US-0591381.
XX
PA   (UNIV ) UNIV KANSAS MEDICAL CENT.
PA   (UNIV ) UNIV KANSAS STATE RES FOUND.
XX
PI   Iwamoto T;  Sullivan LP,  Tomich JM;
XX
DR   WPI; 1997-393366/36.
XX
PT   Channel assembly for transporting ions across epithelial cell
PT   membranes - comprises new water soluble peptide(s), for treating
PT   cystic fibrosis and polycystic kidney disease by altering water flux
PT   across cells
XX
PS   Claim 31; Page 50; 93pp; English.
XX
CC   This M2GlyR peptide is a channel-forming amphipathic helical segment. It
CC   has the amino acid sequence of the putative transmembrane segment M2 of
CC   the strychnine-binding alpha subunit of the inhibitory glycine receptor.
CC   This is used to construct a novel channel assembly, comprising 3-6 novel
CC   peptides, of 18-30 amino acids. The peptides are synthesized by standard
CC   solid phase peptide synthesis. The peptides are water soluble to at
CC   least 10 mM and enables anions to be transported through a membrane of
CC   an epithelial cell when they are embedded in the membrane. The channel
CC   assembly can be used to alter the flux of water across an epithelial
CC   cell, particularly for treatment of cystic fibrosis (where affected cells
CC   are in the airway, pancreatic duct or epididymis). The channel assembly
CC   can also be used in the treatment of autosomal dominant polycystic kidney
CC   disease (where the affected cells are in the cystic epithelium). The
CC   channel assembly spontaneously inserts into the basolateral membrane to
CC   prevent water flow to adjacent cysts.
XX
SQ   Sequence   23 AA;


  Query Match             100.0%;  Score 110;  DB 18;  Length 23;
  Best Local Similarity   100.0%;  Pred. No. 4.6e-11;
  Matches   23;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy       1 PARVGLGITTVLTMTTQSSGSRA 23
           |||||||||||||||||||||||
Db       1 parvglgittvltmttqssgsra 23
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